

CLAIMS

5 1. Apparatus for obtaining an image of a specimen by optical projection tomography, the apparatus comprising light scanning means, a rotary stage for rotating the specimen to be imaged, an optical system and a light detector, wherein light from the scanning means scans the specimen and the optical system is operative, throughout the scanning movement of the light, to direct onto the detector only light which exits or by-passes

10 the specimen parallel to the beam incident on the specimen.

15 2. Apparatus according to claim 1, wherein the optical system is constituted by a convex lens which causes convergence of light incident thereon and directs onto the detector the light which exits or by-passes the specimen parallel to the beam incident on the specimen.

20 3. Apparatus according to claim 1 or 2, wherein the light detector is constituted by a localised detector.

25 4. Apparatus according to claim 3, wherein the localised detector is one detector of a linear array of detectors, the other detectors of the assay constituting auxiliary detectors which detect scattered and/or refracted light.

5. Apparatus according to claim 3, wherein the localised detector is one detector of a two-dimensional array of detectors, the other detectors of the assay constituting auxiliary detectors which detect scattered and/or refracted light.

30 6. Apparatus according to any of the preceding claims, wherein the rotary stage rotates the specimen to indexed positions in each of which the specimen is in use subjected to a scanning movement of incident light by the scanning means.

7. Apparatus according to claim 6, wherein the scanning means is operative to scan the light in a raster pattern, one complete raster scan being undertaken at each indexed position of the specimen.
- 5 8. Apparatus according to any of the preceding claims, wherein the light scanning means form part of a confocal scanning microscope.
- 10 9. An optical system for use in apparatus for obtaining an image in optical projection tomography, the optical system receiving light from a specimen scanned by a light beam and being operative to direct onto a detector only light which exits or by-passes the specimen parallel to the beam incident on the specimen.
- 15 10. A method of obtaining an image of a specimen in optical projection tomography, the method comprising moving a light beam across the specimen with a scanning motion, passing the light emanating from the specimen onto a detector which, throughout the scanning movement of the light, detects light which exits or by-passes the specimen parallel to the beam incident on the specimen.
- 20 11. A method of performing any one or more of the analyses or procedures listed hereunder comprising use of a method or apparatus according to any of claims 1 to 10:
 - Analysis of the structure of biological tissues.
 - Analysis of the function of biological tissues.
 - 25 Analysis of the shapes of biological tissues.
 - Analysis of the distribution of cell types within biological tissues.
 - Analysis of the distribution of gene activity within biological tissues,
including the distribution of:
 - RNA transcripts
 - 30 - proteins
 - Analysis of the distribution of transgenic gene activity within biological tissues,

Analysis of the distribution of cell activities within biological tissues,
including:

- Cell cycle status including arrest
- Cell death
- 5 - Cell proliferation
- Cell migration

Analysis of the distribution of physiological states within biological tissues.

Analysis of the results of immunohistochemistry staining techniques.

Analysis of the results of in-situ hybridisation staining techniques.

10 Analysis of the distribution of molecular markers within biological tissues,
including any coloured or light-absorbing substances, such as:

- 5,5'-dibromo-4,4'-dichloro-indigo (or other halogenated indigo compounds)
- formazan
- or other coloured precipitates generated through the catalytic activity of enzymes

15 including: b-galactosidase, alkaline phosphatase or other coloured precipitates formed upon
catalytic conversion of staining substrates,

- including: Fast Red, Vector Red
- And including any light-emitting substances,
- Therefore including any fluorescent substances,
- 20 such as: Alexa dyes, FITC, rhodamine,
- And including any luminescent substances,
- such as green fluorescent protein (GFP) or similar proteins,
- And including any phosphorescent substances.

25 Analysis of tissues from all plant species.

Analysis of any tissue for agricultural research,

including:

- basic research into all aspects of plant biology (genetics, development, physiology,
pathology etc.)

30 analysis of tissues which have been genetically altered.

Analysis of tissues from all animal species.

including:

invertebrates

nematode worms

vertebrates

5 all types of fish (including teleosts, such as zebrafish, and chondryctyes including sharks)

amphibians (including the genus *Xenopus* and axolotls)

reptiles

10 birds (including chickens and quails)

all mammals (including all rodents, dogs, cats and all primates, including human)

Analysis of embryonic tissues for any purpose,

including:

15 research into any stem cell population

research into developmental biology

research into the causes of abnormal embryo development, including human syndromes

20 autopsies of human terminated pregnancies (both spontaneous and induced terminations)

Analysis of any tissues for the purpose of genomics research,

including:

25 the analysis of any tissues for the purpose of genomics research,

including:

the analysis of transgenic, knock-in, knock-down or knock-out organisms

the analysis or discovery of the expression (or activity) of genes including their spatial distribution, and their levels of expression

30 the analysis or discovery of abnormalities in the structure or morphology of tissues, as a result of interference due to wilful experimentation (such as genetic or physical modifications including a chemical or biochemical

genomics approach), and/or spontaneous abnormalities (such as naturally-occurring mutations)

Analysis of any tissue for the purpose of neurobiology research,

5 including:

- the analysis of the morphology of nerves
- the analysis of the pathways and connectivity of nerves
- the analysis of parts of, or whole, animal brains

10 Analysis of any tissue for pharmaceutical research,

including:

- the analysis of pharmaceutical substances (such as drugs, molecules, proteins, antibodies),

including their spatial distribution within the tissue, and their concentrations

15 the analysis or discovery of abnormalities in the structure or morphology of tissues.

Analysis of tissues for medical research,

including:

- research into the genetics, development, physiology, structure and function of animal tissues

20 analysis of diseased tissue to further our understanding of all types of diseases

including:

- congenital diseases
- acquired diseases

25 including:

- infectious
- neoplastic
- vascular
- inflammatory

30 traumatic

metabolic

endocrine
degenerative
drug-related
iatrogenic or
idiopathic diseases

5 idiopathic diseases

Analysis of tissues for medical diagnosis, treatment or monitoring, including:

the diagnosis of cancer patients

10 including:

searching for cancerous cells and tissues within biopsies

searching for abnormal structure or morphology of tissues within biopsies

the analysis of all biopsies

including the analysis of:

15 lymph nodes

polyps

liver biopsies

kidney biopsies

prostate biopsie

muscle biopsies

20 muscle biopsies

brain tissue

the analysis of tissue removed in the process of extracting a tumour from a patient

including:

determining whether all the tumour has been removed

25 determining the type of tumour, and the type of cancer.

12. Use of a method or apparatus as described in any of claims 1 to 10 in any one or more of the analyses or procedures listed hereunder:

30 Analysis of the structure of biological tissues.

Analysis of the function of biological tissues.

Analysis of the shapes of biological tissues.

Analysis of the distribution of cell types within biological tissues.

Analysis of the distribution of gene activity within biological tissues,
including the distribution of:

5 - RNA transcripts
 - proteins

Analysis of the distribution of transgenic gene activity within biological tissues,

Analysis of the distribution of cell activities within biological tissues,
including:

10 - Cell cycle status including arrest
 - Cell death
 - Cell proliferation
 - Cell migration

Analysis of the distribution of physiological states within biological tissues.

15 Analysis of the results of immunohistochemistry staining techniques.

Analysis of the results of in-situ hybridisation staining techniques.

Analysis of the distribution of molecular markers within biological tissues,
including any coloured or light-absorbing substances, such as:

20 5,5'-dibromo-4,4'-dichloro-indigo (or other halogenated indigo compounds)
 formazan
 or other coloured precipitates generated through the catalytic activity of enzymes
including: b-galactosidase, alkaline phosphatase or other coloured precipitates formed upon
catalytic conversion of staining substrates,
including: Fast Red, Vector Red

25 And including any light-emitting substances,
 Therefore including any fluorescent substances,
 such as: Alexa dyes, FITC, rhodamine,
 And including any luminescent substances,
 such as green fluorescent protein (GFP) or similar proteins,
 And including any phosphorescent substances.

Analysis of tissues from all plant species.

Analysis of any tissue for agricultural research,
including:

5 basic research into all aspects of plant biology (genetics, development, physiology,
pathology etc.)
analysis of tissues which have been genetically altered.

Analysis of tissues from all animal species.

including:

10 invertebrates
nematode worms
vertebrates
all types of fish (including teleosts, such as zebrafish, and chondryctyes including
sharks)
15 amphibians (including the genus Xenopus and axolotls)
reptiles
birds (including chickens and quails)
all mammals (including all rodents, dogs, cats and all primates, including human)

20 Analysis of embryonic tissues for any purpose,

including:

research into any stem cell population
research into developmental biology
research into the causes of abnormal embryo development, including human
25 syndromes
autopsies of human terminated pregnancies (both spontaneous and induced
terminations)

Analysis of any tissues for the purpose of genomics research,

30 including:

the analysis of any tissues for the purpose of genomics research,

including:

the analysis of transgenic, knock-in, knock-down or knock-out organisms
the analysis or discovery of the expression (or activity) of genes including
their spatial distribution, and their levels of expression

5 the analysis or discovery of abnormalities in the structure or morphology of
tissues, as a result of interference due to wilful experimentation (such as
genetic or physical modifications including a chemical or biochemical
genomics approach), and/or spontaneous abnormalities (such as naturally-
occurring mutations)

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Analysis of any tissue for the purpose of neurobiology research,

including:

the analysis of the morphology of nerves
the analysis of the pathways and connectivity of nerves
15 the analysis of parts of, or whole, animal brains

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Analysis of any tissue for pharmaceutical research,

including:

20 the analysis of pharmaceutical substances (such as drugs, molecules, proteins,
antibodies),
including their spatial distribution within the tissue, and their concentrations
the analysis or discovery of abnormalities in the structure or morphology of tissues.

20

Analysis of tissues for medical research,

25 including:

research into the genetics, development, physiology, structure and function of
animal tissues

analysis of diseased tissue to further our understanding of all types of diseases

including:

30 congenital diseases

acquired diseases

including:
infectious
neoplastic
vascular
5 inflammatory
traumatic
metabolic
endocrine
degenerative
10 drug-related
iatrogenic or
idiopathic diseases

Analysis of tissues for medical diagnosis, treatment or monitoring,

15 including:
the diagnosis of cancer patients

including:
searching for cancerous cells and tissues within biopsies
searching for abnormal structure or morphology of tissues within biopsies

20 the analysis of all biopsies
including the analysis of:

lymph nodes
polyps
liver biopsies
25 kidney biopsies
prostate biopsies
muscle biopsies
brain tissue

the analysis of tissue removed in the process of extracting a tumour from a patient
30 including:
determining whether all the tumour has been removed

determining the type of tumour, and the type of cancer.